REMARKS

In the present Application, Claims 1-6, 8-26 and 28-35 are currently pending, while Claims 36-47 have been withdrawn from consideration. In the instant Office Action, the Examiner has raised several issues, which are set forth below in the order they are addressed herein:

1) Claims 1, 6, 10-12, 18, 19, 24 and 31 are objected to for various informalities and as allegedly being in improper dependent form;
2) Claims 6, 8-26 and 28-35 stand rejected under 35 USC § 112, first paragraph, as allegedly lacking enablement;
3) Claims 1-6, 8-26 and 28-35 stand rejected under 35 USC § 112, second paragraph, as allegedly being indefinite;
4) Claims 1 and 2 stand rejected under 35 USC § 102(a), as allegedly anticipated by Thiel *et al.*, J Gen Virol, 84:2305-2315, 2003 (Thiel) or Snijder *et al.*, J Molec Biol, 331:991-1004, 2003 (Snijder); and
5) Claims 1-5 stand rejected under 35 USC § 102(a), as allegedly anticipated by Yount *et al.*, Proc Natl Acad Sci USA, 100:12995-1300, 2003 (Yount).

Applicants thank the Examiner for consideration of the Information Disclosure Statement and for indicating that Claims 6, 8-26 and 28-35 appear to be free of the prior art. Applicants hereby cancel Claims 1-5, 11, 15 and 36-44, amend Claims 6, 10, 12, 18, 24, 33 and 35, and enter new Claims 48-51, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments. Applicants reserve the right to prosecute the original, similar, or broader claims in one or more future application(s). The amendments do not introduce new matter and do not narrow the scope of any of the claims within the meaning of *Festo*.[1]

1) The Claims Are Proper

The Examiner has objected to Claims 1, 6, 10-12, 18, 19, 24 and 31. In the first place, the Examiner has requested correction of informalities in Claims 1, 6, 18 and 24. Accordingly,

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[1] *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 122 S.Ct. 1831, 1838, 62 USPQ2d 1705, 1710 (2002).

Applicants have amended canceled Claim 1 and amended Claims 6, 18 and 24 to recite "presence of" and "primary rhesus monkey kidney (pRHMK)" as requested by the Examiner.

In the second place, the Examiner has indicated that Claims 10-12, are improper for allegedly failing to further limit the subject matter of the base claim upon which the depend. Although Applicants respectfully disagree, Applicants hereby cancel Claim 11 and amend Claims 6, 18 and 24 to recite "cells chosen from human embryonic kidney (HEK)-293, HEK-293T, Huh-7, Mv1Lu, Mv1Lu-hf and primary rhesus monkey kidney (pRHMK) cells." In addition, Applicants hereby amend Claims 10 and 12, and enter new Claims 48-51 to recite individual cell lines from the group listed in the independent Claim 6. Support for the amendments and new claims is found for instance in Example 1, which lists exemplary cell lines for use with the methods of the present invention, and in the description which teaches that in "one embodiment, the transgenic cell is a Mv1Lu-hF cell (ATCC accession No. PTA-4737), i.e., a transgenic Mv1Lu that expresses human furin" (Specification, at paragraph [0149]).

In the third place, the Examiner has indicated that Claims 19 and 31 are improper for allegedly failing to further limit the subject matter of the base claim upon which the depend. Although Applicants respectfully disagree, Applicants hereby amend Claims 18 and 24 to recite "one or both of" SARS-coronavirus genomic RNA and subgenomic RNA, "one or both of" first and second treated samples, and "one or both of" treated and untreated cells, respectively. Support for these amendments is found for example, in original Claims 18, 19, 24 and 31, and in sections G and H of the description, which discloses methods for detecting replication of SARS-CoV and methods for screening anti-SARS-CoV agents. In particular, the description teaches methods comprising "detecting the presence of one or more of SARS-coronavirus gRNA and SARS-coronavirus sgRNA" (Specification, at paragraph [0209]).

2) The Claims Are Enabled

The Examiner has rejected Claims 6, 8-26 and 28-35 under 35 USC § 112, first paragraph, as allegedly lacking enablement. The Examiner states

> it is apparent that cell lines HEK-293T, Huh-7 and Mv1Lu are required to practice the claimed invention, because they are specifically recited in the claims...The specification does not provide a repeatable method for obtaining these specific cell lines, and it does not appear to be readily available material" (Office Action, page 3).

Applicants respectfully disagree that the claims lack enablement, since all of the recited cell lines are readily available to the public. Human embryonic kidney (HEK) 293 cells are a cell line transformed by exposure to sheared fragments of adenovirus type 5 DNA as described by Graham *et al.*, J Gen Virol, 36:59-74 (1977). HEK 293 cells are available from American Type Culture Collection (ATCC) of Manassa, Virginia, as catalog number CRL-1573. The HEK 293T (also known as 293/tsA1609neo) cells are a cell line derived from HEK 293 cells by insertion of the temperature-sensitive SV40 T antigen as described by Dubridge *et al.*, Mol Cell Biol, 7:379-387 (1987). HEK 293T cells are available from ATCC with written authorization from Michele Calos, and from the Interlab Cell Line Collection (ICLC) of Genova, Italy, as catalog number ICLC HTL04001. Huh-7 (also known as JTC-39) cells are a human hepatoma cell line established from a hepatocellular carcinoma as described by Nakabayashi *et al.*, Cancer Res, 42:3858-63 (1982). Huh-7 cells are available from the Japanese Collection of Research Bioresources (JCRB) of Tokyo, Japan, as catalog number JCRB0403. Lastly, Mv1Lu (also known as NBL-7) cells are an epithelial cell line derived from fetal mink lung cells as described by Henderson *et al.*, Virology, 60:282-287 (1974). Mv1Lu cells are available from ATCC as catalog number CCL-64. This information is included in Example 1 of the instant application (Specification, updated Table 3 and description thereof). Accordingly, Applicants respectfully request that this rejection be withdrawn.

3) The Claims Are Definite

The Examiner has rejected Claims 1-6, 8-26 and 28-35 under 35 USC § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner has lodged rejections against Claims 1, 2, 15, 18-21, 24, 31 and 33. Although Applicants respectfully disagree that the claims as written are indefinite, Applicants hereby cancel Claims 1, 2 and 15, and amend Claims 18, 24, 33 and 35, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). Specifically, Applicants have amended Claims 18 and 24 as detailed above in Section 1, to recite "one or both of" SARS-coronavirus genomic RNA and subgenomic RNA, "one or both of" first and second treated samples, and "one or both of" treated and untreated cells, respectively. In addition, Applicants have amended Claims 33 and 35 to recite "a second test agent."

In regards to Claims 18-21 the Examiner states:

> the purpose of the assay is not apparent, why detect virus from two samples? What useful information is gained by determining that patient Smith's sample has more subgenomic RNA than patient Doe's sample...? Are claims 18-23 actually meant to involve comparing the results of different treatments for one divided virus sample?"

Applicants respectfully draw the Examiner's attention to the description, which discloses:

> methods for detecting the presence of SARS-CoV in one or more samples, such as in samples from mammals that have been treated with anti-SARS-CoV agents. These methods may be used in, for example, determining the efficacy of a therapeutic modality (such as a chemical drug) in reducing SARS-coronavirus infection in a mammal, including a model animal and human. These methods are also useful in determining the relative efficacy of different therapeutic modalities, such as different concentrations of the same drug, the same concentration of different drugs, and different combinations of drugs (Specification, at paragraph [0208]).

Thus in some embodiments, the present invention provides tools for measuring titers of infectious virus from multiple samples obtained from a single subject (e.g., before and after SARS-CoV infection, before and after treatment for SARS, blood sample versus lung cell sample, etc.). In other embodiments, the present invention provides tools for comparing viral titers in multiple samples obtained from multiple subjects (e.g., testing a population of individuals exposed to SARS, testing SARS-infected subjects receiving a placebo or an experimental therapy).

In regard to Claim 24, the Examiner states:

> Claim 24 is confusing, because it calls for detecting an altered level of SARS replication without any step of infecting the treated cells with SARS, and it does not state whether or not the "cells not treated with said first test agent" are the same kind of cells as the treated cells (Office Action, page 5).

Although, Applicants respectfully disagree that the claims are indefinite, for the sake of clarity, Applicants have amended Claim 24 to recite a step of "treating said cells with a sample comprising SARS-coronavirus before or after incubating said cells in the presence and absence of a first test agent." Support for this amendment is found for instance in the description, which teaches that this:

> method may be used in, for example, screening anti-SARS-coronavirus drugs. Anti-SARS-coronavirus drugs may be used as prophylactic agents and/or therapeutic agents in the treatment of SARS-coronavirus. ... The invention's methods are also useful in determining the efficacy of a drug in reducing infection in a model mammal and in human clinical trials (Specification, at paragraph [0218].

Thus in some embodiments, the present invention provides tools for assessing the ability of a test compound to prevent SARS CoV infection (e.g., prophylactic), while in others the present invention provides tools for assessing the ability of a test compound to treat an established SARS CoV infection (e.g., therapeutic). In still further embodiments, the present invention provides tools for comparing the efficacy of test compounds to prevent or treat SARS CoV infection.

As the amended claims are definite, Applicants respectfully request that this rejection be withdrawn.

4 & 5) The Claims are Novel over Thiel, Snijder and Yount

The Examiner has rejected Claims 1 and 2 under 35 USC § 102(a), as allegedly anticipated by Thiel et al., J Gen Virol, 84:2305-2315, June 19, 2003 (Thiel) or Snijder et al., J Molec Biol, 331:991-1004, August 20, 2003 (Snijder); and has rejected Claims 1-5 stand rejected under 35 USC § 102(a), as allegedly anticipated by Yount et al., Proc Natl Acad Sci USA, 100:12995-1300, October 20, 2003 (Yount). In particular, the Examiner contends that each of these three publications teaches methods of detecting SARS infection by detecting SARS coronavirus subgenomic RNA before Applicants' November 3, 2003 filing date. Although, Applicants respectfully disagree that the claims are anticipated, Applicants have canceled Claims 1-5, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). Accordingly, these rejections are rendered moot.

CONCLUSION

Applicants believe the arguments and amendments set forth above traverse the Examiner's rejections and, therefore request that a timely Notice of Allowance be issued in this case. However, should the Examiner believe that a telephone interview would aid in the

prosecution of this application, Applicants encourage the Examiner to call the undersigned collect.

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